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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,149	11/01/2001	C. Frank Bennett	RTS-0325	4677

7590 03/04/2004

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EXAMINER	
SCHULTZ, JAMES	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 03/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/016,149	BENNETT ET AL.	
	Examiner	Art Unit	
	J. Douglas Schultz	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-10 and 12-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5-10, 12-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

1. Applicant's response filed February 9, 2004 has been considered. Rejections and/or objections not reiterated from the previous office action mailed November 18, 2003 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previously Indicated Allowable Subject Matter

3. Applicants have amended claim 1, canceled claims 2-4, and amended depended claims to depend from claim 1. This was in response to an objection set forth in the previous Office action to claims 4-10, 13, and 15, said objection indicating that claims 4-10, 13, and 15 would be allowable if re-written in independent form. However, the indication of allowability is withdrawn in view of the rejection that follows. Applicants submitted arguments that are relevant to the new rejection are addressed below.

Claim Rejections - 35 USC § 103

Claims 1, 5-10, and 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tischfield et al., in view of Balboa et al., Taylor et al., and Baracchini et al. (all of record).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The invention of the above claims is drawn to antisense compounds targeted to nucleobases 586 to 903 of a 3'-untranslated region of phospholipase A2 group V (applicants' instant SEQ ID NO: 3), or said compounds comprising internucleoside, sugar, nucleobase, and 2' modifications, chimeras, or compositions comprising said compounds and pharmaceutically acceptable diluents thereof, and methods of their use *in vitro*.

At the outset, it is noted that table 1 of the specification identifies the 3' untranslated region as comprising nucleotides 570 to 989, which corresponds to virtually the entire region instantly claimed by applicants, i.e. 586 to 903 of SEQ ID NO: 3. Because applicants instantly claimed target region corresponds to most of the 3'-UTR, and because one of ordinary skill in the art would know that it is obvious to generate antisense oligos to target the 3'-UTR for antisense-mediated gene inhibition, the above listed claims are considered to be obvious as detailed below.

Tischfield et al. teach antisense inhibition of SEQ ID NO: 3, and also teach the sequence encoding phospholipase A2 group V (i.e. applicants' instant SEQ ID NO: 3). Tischfield et al. do not teach oligonucleotides 8 to 50 nucleobases that comprise internucleoside, sugar, nucleobase,

chimeras, and 2' modifications, or compositions comprising said compounds and pharmaceutically acceptable diluents thereof.

Balboa et al. teach an antisense compound 21 nucleotides in length, wherein said compound is in a composition comprising a pharmaceutical diluent and a method of using said compound to target inhibit the expression of murine phospholipase A2 group V, which is homologous with applicant's instant claimed target of SEQ ID NO: 3.

Taylor et al. teach the inhibition of expression of any protein using a known cDNA sequence to generate antisense oligos that target and inhibit the expression of that protein, and also teach that with software analysis and high affinity oligos, one needs to screen only 3-6 oligos to find one that inhibits its target 66-95% (p. 565).

Baracchini et al. teach modifications of antisense compounds comprising the specific sugar, nucleobase, 2' modifications, chimeras, and compositions comprising said compounds and pharmaceutically acceptable diluents thereof identical to those claimed by applicants. Baracchini et al. also teach targeting specific regions of a gene including the 3'-untranslated region, and disclose precise methods necessary to achieve antisense-mediated gene inhibition, including synthesis protocols, starting reagents, equipment and reagent manufacturers, and assays for determining antisense efficacy.

It would have been obvious to one of ordinary skill in the art to take the antisense sequences of Tischfield, that target the cDNA sequence of phospholipase A2 group V and syntehsize them 8 to 50 nucleotides long with modifications to prolong their half-life as taught by Balboa, Baracchini and Taylor for inhibition of phospholipase A2 group V expression.

One would have been motivated to create such compounds because Tischfield et al. expressly teach antisense inhibition of applicants' instant phospholipase A2 group V target of SEQ ID NO: 3, and further, because Balboa et al. expressly teach antisense-mediated-inhibition of the homologous murine homologue *in vitro* using an antisense oligonucleotides 21 nucleobases in length in a method of interfering with a cellular signaling pathway related to inflammation. Balboa et al. further teach that phospholipase A2 group V is involved in "diverse pathologic processes, such as rheumatoid arthritis, septic shock, intestinal neoplasia, and epidermal hyperplasia..." See abstract. Therefore, one of ordinary skill would have been motivated to inhibit phospholipase A2 group V in order to examine the consequences of its inhibition on this diverse list of biological processes. One of skill would have been motivated to target nucleobases 586 to 903 of the phospholipase A2 group V mRNA transcript, because this region corresponds to virtually the entire 3'-untranslated region (see applicants table 1) and because Baracchini et al. teach that the 3'-untranslated region is a preferred region for targeting antisense to, and also exemplify its targeting. One would have been motivated to modify said antisense compounds as taught by Baracchini et al. and Taylor et al., because Baracchini et al. teach that such antisense modifications increase an antisense compound's cellular uptake, target affinity and resistance to degradation, and because Taylor et al. teach that modifications are routinely made to oligonucleotides to take advantage of their longer bioactive half-life. .

One of ordinary skill would have had a reasonable expectation of success in targeting the 3'-untranslated region as claimed by applicants, because Baracchini et al. show that inhibition of the 3'-untranslated region of their target gene results in a high level of inhibition (see Table 1 of Baracchini et al.), and further because Taylor et al. teach that with software analysis and high

affinity oligos, one needs to screen only 3-6 oligos to find one that inhibits its target 66-95% *in vitro*. Finally, one of ordinary skill would have had a reasonable expectation of success in making and using the modified oligos claimed by applicants, since Baracchini et al. teach making modified antisense compounds targeted to distinct regions of a target gene, and include all reagents and suppliers, equipment manufacturers, and assays needed to test for phospholipase A2 group V inhibition, and because the steps therein are routine to one of ordinary skill in the art.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz whose telephone number is 571-272-0763. The examiner can normally be reached on 8:00-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 703-308-0447. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James Douglas Schultz, PhD

SEAN McGARRY
PRIMARY EXAMINER
1635